

### **Listing of Claims**

This listing of claims will replace all prior versions and listings of claims in the Application.

1. (Previously Presented) A method for making microspheres comprising a bioactive substance, the method comprising:

dissolving a polymer with an organic solvent to produce a polymer solution;

adding a biologically effective amount of a bioactive substance to the polymer solution to produce a mixture of the polymer and the bioactive substance, wherein no additional processing medium is required;

vibrating the mixture to produce a bioactive substance-polymer complex;

emulsifying the mixture to produce an emulsion comprising the bioactive substance-polymer complex; and

extracting the organic solvent from the emulsion to produce microspheres comprising the polymer-bioactive substance complex, wherein the bioactivity of the bioactive substance is usefully preserved and wherein no additional emulsification or mechanical agitation is performed.

2. (Original) The method of Claim 1, wherein the microspheres are biodegradable and biocompatible.

3. (Original) The method of Claim 1, wherein the bioactive substance comprises a therapeutic agent.

4. (Original) The method of Claim 1, wherein the bioactive substance comprises a drug.

5. (Original) The method of Claim 1, wherein the bioactive substance comprises a polypeptide.

6. (Original) The method of Claim 1, wherein the bioactive substance is a solid.

7. (Original) The method of Claim 1, wherein the bioactive substance is selected from the group consisting of nerve growth factor, interferon, growth hormone, insulin, erythropoietin, transforming growth factor, epidermal growth factor, interleukin-2, basic fibroblast growth factor and VEGF.

-

8. (Original) The method of Claim 1, the method further comprising stabilizing the bioactive substance.

9. (Original) The method of Claim 8, wherein the bioactive substance is stabilized with a carrier protein.

10. (Original) The method of Claim 9, wherein the carrier protein comprises albumin.

11. (Original) The method of Claim 8, wherein the bioactive substance is stabilized by maximizing the concentration of the substance in the solution, by adding a metal to the solution, by adding gelatin to the solution, or by adding a small osmolyte to the solution.

12. (Original) The method of Claim 1, wherein the polymer comprises a combination of PLGA and PEG, wherein PEG comprises approximately 1% by weight of the combination.

13. (Original) The method of Claim 1, wherein the organic solvent comprises methyl chloride.

14. (Original) The method of Claim 1, wherein the mixture is emulsified with polyvinyl alcohol.

15. (Original) The method of Claim 1, wherein the emulsion is extracted with polyvinyl alcohol and isopropyl alcohol.

16. (Original) The method of Claim 1, the method further comprising removing the microspheres from the extracted emulsion.

17. (Original) The method of Claim 16, wherein the microspheres are removed from the extracted emulsion by centrifugation.

18. (Previously Presented) The method of Claim 16, the method further comprising washing, freezing and lyophilizing the removed microspheres.

19. (Canceled)

20. (Canceled)

21. (Canceled)

22. (Canceled)

23. (Previously Presented) A method for making microspheres comprising a solid bioactive substance, the method comprising:

dissolving a polymer with an organic solvent to produce a polymer solution;

adding a biologically effective amount of a solid bioactive substance to the polymer solution to produce a mixture of the polymer and the bioactive substance, wherein no additional processing medium is required;

vibrating the mixture to produce a bioactive substance-polymer complex;

emulsifying the mixture to produce an emulsion comprising the bioactive substance-polymer complex; and

extracting the organic solvent from the emulsion to produce microspheres comprising the polymer-bioactive substance complex, wherein the bioactivity of the bioactive substance is usefully preserved and wherein no additional emulsification or mechanical agitation is performed.

24. (Previously Presented) A method for microencapsulating a bioactive substance, the method comprising:

providing a bioactive substance;

providing at least one polymer;

providing an organic solvent;

dissolving the polymer in a volume of the organic solvent to produce a polymer solution;

adding the bioactive substance to the solution to produce a mixture of the polymer and the bioactive substance, wherein no additional processing medium is required;

vibrating the mixture to produce a bioactive substance-polymer complex;

emulsifying the mixture to produce an emulsion comprising the bioactive substance-polymer complex; and

extracting the organic solvent from the emulsion to produce microspheres comprising the polymer-bioactive substance complex, wherein the biological activity of the bioactive substance is substantially preserved and wherein no additional emulsification or mechanical agitation is performed.

25. (Original) Microspheres made according to the method of Claim 1.

26. (Original) The microspheres of Claim 25, wherein the microspheres are biodegradable.

27. (Original) The microspheres of Claim 25, wherein the microspheres comprise a therapeutic agent.

28. (Original) The microspheres of Claim 27, wherein the therapeutic agent is selected from the group consisting of nerve growth factor, interferon, growth hormone, insulin,

erythropoietin, transforming growth factor, epidermal growth factor, interleukin-2, basic fibroblast growth factor and VEGF.

29. (Original) The microspheres of Claim 25, wherein the microspheres comprise a polypeptide.

30. (Original) The microspheres of Claim 25, wherein the microspheres comprise a drug.

31. (Original) Microspheres made according to the method of Claim 23.

32. (Original) The microspheres of Claim 31, wherein the microspheres are biodegradable and biocompatible.

33. (Original) The microspheres of Claim 31, wherein the microspheres comprise a therapeutic agent.

34. (Original) The microspheres of Claim 33, wherein the therapeutic agent is selected from the group consisting of nerve growth factor, interferon, growth hormone, insulin, erythropoietin, transforming growth factor, epidermal growth factor, interleukin-2, basic fibroblast growth factor and VEGF.

35. (Original) The microspheres of Claim 23, wherein the solid bioactive substance comprises a polypeptide.

36. (Original) The microspheres of Claim 23, wherein the microspheres comprise a drug.

37. (Previously Presented) A method for making microspheres comprising a bioactive substance, the method consisting of:

dissolving a polymer with an organic solvent to produce a polymer solution;

adding a biologically effective amount of a bioactive substance to the solution to produce a mixture of the polymer and the bioactive substance;

vibrating the mixture to produce a bioactive substance-polymer complex;

emulsifying the mixture to produce an emulsion comprising the bioactive substance-polymer complex; and

extracting the organic solvent from the emulsion to produce microspheres comprising the polymer-bioactive substance complex, wherein the bioactivity of the bioactive substance is usefully preserved and wherein no additional emulsification is performed.

38. (Previously Presented) A method for making microspheres comprising a solid bioactive substance, the method consisting of:

dissolving a polymer with an organic solvent to produce a polymer solution;

adding a biologically effective amount of a solid bioactive substance to the solution to produce a mixture of the polymer and the bioactive substance;

vibrating the mixture to produce a bioactive substance-polymer complex;

emulsifying the mixture to produce an emulsion comprising the bioactive substance-polymer complex; and

extracting the organic solvent from the emulsion to produce microspheres comprising the polymer-bioactive substance complex, wherein the bioactivity of the bioactive substance is usefully preserved and wherein no additional emulsification is performed.

39. (Previously Presented) A method for microencapsulating a bioactive substance, the method consisting of:

providing a bioactive substance;

providing at least one polymer;

providing an organic solvent;

dissolving the polymer in a volume of the organic solvent to produce a polymer solution;

adding the bioactive substance to the solution to produce a mixture of the polymer and the bioactive substance;

vibrating the mixture to produce a bioactive substance-polymer complex;

emulsifying the mixture to produce an emulsion comprising the bioactive substance-polymer complex; and

extracting the organic solvent from the emulsion to produce microspheres comprising the polymer-bioactive substance complex, wherein the biological activity of the bioactive substance is substantially preserved and wherein no additional emulsification is performed.